Remarks

Claims 1-25 and 32-34 are pending. Claims 26-30 have been withdrawn. Claim 4 has been amended. Claims 2-3 have been canceled.

Rejection of claims 1, 5, 7-25 and 31-33

Claims 1, 4, 5, 7-25 and 31-33 stand rejected based on the contention that they are obvious over the combined teachings of Cho-Chung (U.S. Patent No. 5,271,941); Zhou et al. (WO 99/50409); Agrawal (WO 97/11171) and Tsuchiya (WO 96/196967) in view of McKay et al. (U.S. Patent No. 6,133,246) and Wang (U.S. 5,858,988). Applicants respond as follows.

Cho-Chung (U.S. Patent No. 5,271,941)

It is asserted in the Office Action that Cho-Chung teaches olignonucleotides of between 21-23 nucleotides in length that target the expression of RIα/PKA in cells in vitro and reduce cancer cell growth in vivo, and SEQ ID NO:2 of Cho-Chung is pointed out as an example of such an oligonucleotide.

In response, Applicants point out that **SEQ ID NO:2** in Cho Chung is not an oligoribonucleotide consisting from 21 to 23 nucleotides. Further, SEQ ID NO:2 of Cho Chung was not tested in vitro or in vivo in Cho Chung (see, for example, Figures 1-7 of Cho Chung). **SEQ ID NO:1** of Cho Chung was tested, but the sequence of this oligonucleotide is different from SEQ ID NO:1 of the present application in 13 out of 21 positions, and Applicants therefore submit that one skilled in the art would not expect this oligonucleotide to bind to the same RIα/PKA target sequence as the presently claimed sequences. Further, the present application expressly distinguishes the instant invention from SEQ ID NO:2 of Cho Chung by disclosing that an oligonucleotide with sequence GCGUGCCTCCTCACUGGC (i.e., SEQ ID NO:2 in Cho Chung) was shown to inhibit the growth of cancer cells with an IC_{50} value of 100 nM. However, it is disclosed in the present specification as filed that by adding GGCU at the 5'-end and deleting C at the 3'-end of sequence GCGUGCCTCCTCACUGGC and replacing its mixed backbone by a poly-DNP platform, the inhibition efficacy was increased 20 to 100-fold (see

paragraph spanning pages 4-5 of the instant specification). In connection with this, Applicants respectfully submit that there is nothing in the record to support that that adding GGCU at the 5'-end and deleting C at the 3'-end of the sequence GCGUGCCTCCTCACUGGC is an obvious modification of SEQ ID NO:2 (or SEQ ID NO:1) of Cho Chung, or of any of the other cited sequences.

Zhou et al. (WO 99/50409)

With respect to Zhou et al. (WO 99/50409), it appears the only sequences disclosed in this reference are provided in Table 1. However, it also appears that none of the nucleotide sequences of these oligonucleotides match that in the sequence alignment provided by the Examiner and attributed to Zhou et al. Rather, the sequence in the alignment appears to be a 3'-5' orientation of olignonucleotides 1 and 2 in Table 1 in Zhou et al., but is missing a terminal C, and does not appear to be from 21 to 23 nucleotides in length. Further, Applicants are unclear as to the source of the accession number attributed to the oligonucleotide sequence of Zhou et al. Nevertheless, insofar as Zhou et al. refers to RIα, it is indicated that oligo 1 in Table 1 is complementary to the RIα regulatory subunit of protein kinase A and has been studied in both in vitro and in vivo models. However, oligos 1 and 2 of Zhou et al. have the same nucleotide sequence as that referenced above as disclosed in Cho Chung. Thus, it is submitted that the disclosure of Zhou et al. does not contribute anything to the art over that disclosed in Cho Chung.

Agrawal (WO 97/11171)

With respect to Agrawal (WO 97/11171), Applicants note that the sequence from Agrawal provided in the sequence alignment provided by the Examiner is the same sequence as SEQ ID NO:2 disclosed in Cho Chung, but has a mixed DNA / RNA backbone. Further, as Applicant has stated above with respect to Cho Chung and to Zhou et al., the present specification expressly discloses that it was discovered that by adding GGCU at the 5'-end and deleting C at the 3'-end of the sequence of Cho Chung (which is the same as the sequence cited

for Agrawal, but without the C at the 3'-end) and replacing its mixed backbone by a poly-DNP platform, the inhibition efficacy was increased 20 to 100-fold. Applicants reiterate that there is nothing in the record in support of the contention that adding GGCU at the 5'-end and deleting a C at the 3'-end the sequence of GCGUGCCTCCTCACUGGC would be an obvious modification of any of the cited oligonucleotides.

Tsuchiya (WO 96/196967)

With respect to the Japanese language reference of Tsuchiya (WO 96/196967), Applicants note that the sequence alignment provided by the Examiner (which appears to correspond to nucleotides 9-29 of SEQ ID NO:5 of Tsuchiya, which is a 30-mer) shows only 76.2% homology with instant SEQ ID NO:1. Therefore, Applicants submit that one skilled in the art would not expect this oligonucleotide to bind to the same sequence as the presently claimed oligonucleotides. Further, it is not clear from the Office Action how the Examiner has concluded that this reference discloses that the cited oligoribonucleotide can inhibit RIα/PKA expression, particularly since the English language abstract refers only generally to a structure (I) which has variable length and complementary to SEQ ID NO:1, which is 300 nucleotides long. Therefore, Applicants submit there is no basis on the record to support that the disclosure of Tsuchiya contributes to a finding of obviousness for the present invention.

McKay et al. (U.S. Patent No. 6,133,246) and Wang (U.S. 5,858,988)

With respect to the citation of McKay et al. (U.S. Patent No. 6,133,246) and Wang (U.S. 5,858,988), Applicants respectfully submit that since the presently claimed sequences are not obvious from the references of Cho-Chung, Zhou et al., Agrawal and Tsuchiya, the additional citation of McKay et al. and Wang is inadequate to render the present claims obvious.

Conclusion

Applicants respectfully submit that, in view of the foregoing, it is believed that none of the cited references alone or in combination render the presently claimed invention obvious, and therefore, all of the claims are now in condition for allowance. The Examiner is thus respectfully requested to remove the rejections and allow all the claims.

Applicants request a one-month extension of time to file this response. A check for for the required fee is enclosed. If any additional fee is due it may be charged to Deposit Account no. 08-2442.

Respectfully submitted,

By: _____
John D. Lopinski, Reg. No. 50,486

HODGSON RUSS LLP
The Guaranty Building
140 Pearl Street, Suite 100
Buffalo, NY 14202-4040
Tel. 716-848-1430

Dated: March 6, 2008

011520/00338 BFLODOCS 2195731v1